

Atty. Dkt. No. 025098-0701

**Listing of the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously presented) A method for designing a specific polyamide



wherein

$X_1$ ,  $X_2$ ,  $X_m$ ,  $X_{(m+1)}$ ,  $X_{(2m-1)}$ , and  $X_{2m}$  are carboxamide residues forming carboxamide binding pairs  $X_1/X_{2m}$ ,  $X_2/X_{(2m-1)}$ ,  $X_m/X_{(m+1)}$ ,

$\gamma$  is  $\gamma$ -aminobutyric acid or 2,4 diaminobutyric acid, and

$R_1$  is  $-\text{NH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ ,  $-\text{NH}(\text{CH}_2)_{0-12}\text{CONH}(\text{CH}_2)_{0-100}\text{NR}_2\text{R}_3$ , or  $-\text{NHR}_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $\text{C}_{1-100}$  alkyl,  $\text{C}_{1-100}$  alkylamine,  $\text{C}_{1-100}$  alkyldiamine,  $\text{C}_{1-100}$  alkylcarboxylate,  $\text{C}_{1-100}$  alkenyl, a  $\text{C}_{1-100}$  alkynyl, and  $\text{C}_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosoarea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrinilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral, suitable for use as a DNA-binding

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ligand that is selective for identified target DNA-sequences  $5' \text{-WN}_1\text{N}_2 \dots \text{N}_m\text{W-3'}$  where  $m$  is an integer having a value from 3 to 6, the method comprising:

(a) identifying a target sequence of double stranded DNA having the form  $5' \text{-WN}_1\text{N}_2 \dots \text{N}_m\text{W-3'}$ ,  $\text{N}_1\text{N}_2 \dots \text{N}_m$  being the sequence to be bound by carboxamide residues, wherein each  $\text{N}$  is independently chosen from the group A, G, C, and T, each  $\text{W}$  is independently chosen from the group A and T, and  $m$  is an integer having a value from 3 to 6;

(b) representing the identified sequence as  $5' \text{-Wab} \dots x\text{W-3'}$ , wherein  $a$  is a first nucleotide to be bound by the  $\text{X}_1$  carboxamide residue,  $b$  is a second nucleotide to be bound by the  $\text{X}_2$  carboxamide residue, and  $x$  is the corresponding nucleotide to be bound by the  $\text{X}_m$  carboxamide residue;

(c) defining  $a$  as A, G, C, or T to correspond to the first nucleotide to be bound by a carboxamide residue in the identified sequence;

(d) selecting  $\text{Im}$  as the  $\text{X}_1$  carboxamide residue and  $\text{Py}$  as the  $\text{X}_{2m}$  carboxamide residue if  $a = \text{G}$ ;

(e) selecting  $\text{Py}$  as the  $\text{X}_1$  carboxamide residue and  $\text{Im}$  as the  $\text{X}_{2m}$  carboxamide residue if  $a = \text{C}$ ;

(f) selecting  $\text{Hp}$  as the  $\text{X}_1$  carboxamide residue and  $\text{Py}$  as the  $\text{X}_{2m}$  carboxamide residue if  $a = \text{T}$ ;

(g) selecting  $\text{Py}$  as the  $\text{X}_1$  carboxamide residue and  $\text{Hp}$  as the  $\text{X}_{2m}$  carboxamide residue if  $a = \text{A}$ ; and

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(h) repeating steps c – g for *b* through *x* until all carboxamide residues are selected; wherein Im is N-methylimidazole, Hp is 3-hydroxy-N-methylpyrrole, Py is N-methylpyrrole, A is adenine, G is guanine, C is cytosine, and T is thymine; and synthesizing the polyamide.

2. (Cancelled)

3. (Previously presented) The method of claim 1 further comprising the step of determining if the binding affinity of the polyamide to the identified target sequence is subnanomolar.

4. (Previously presented) The method of claim 1 further comprising the step of determining if the polyamide exhibits a binding affinity that is at least ten-fold higher for said identified target sequence compared to a non-target DNA sequence.

5. (Previously presented) The method of claim 1 further comprising the step of replacing at least one pyrrole residue with a  $\beta$ -alanine residue.

6-37 (Cancelled)

38. (Previously presented) A polyamide composition produced by the method of claim 1 wherein one carboxamide binding pair is  $\beta/\beta$ , wherein  $\beta$  is  $\beta$ -alanine.

39-41. (Cancelled)

42. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a regulatory sequence.

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43. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a promoter sequence.

44. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a coding sequence.

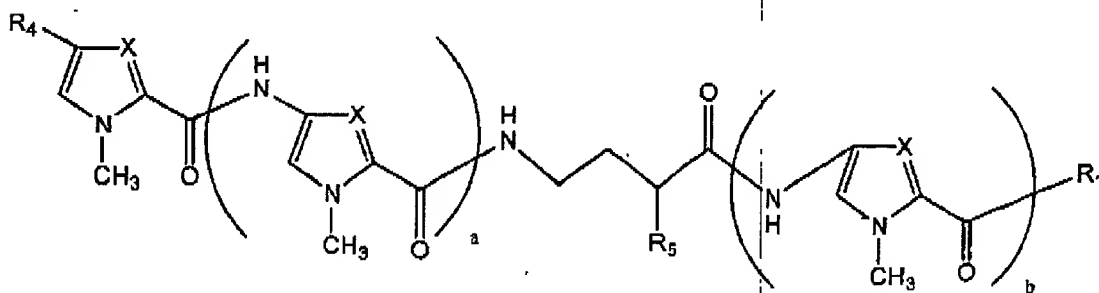
45. (Previously presented) The method of claim 1 wherein the identified target DNA sequence is a non-coding sequence.

46. (Previously presented) A polyamide composition produced by the method of claim 1 wherein the binding of the carboxamide binding pairs to the identified target DNA sequence modulates the expression of a gene.

47. (Previously presented) A composition comprising an effective amount of a polyamide produced by the method of claim 1 and a pharmacologically suitable excipient.

48. (Previously presented) A diagnostic kit comprising a polyamide produced by the method of claim 1.

49. (Previously presented) A polyamide designed by the method of claim 1, having the structure:



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wherein

$R_4$  is selected from the group consisting of H,  $NH_2$ , SH, Cl, Br, F, N-acetyl, and N-formyl;

$R_5$  is H or  $NH_2$ ;

$R_1$  is  $-NH(CH_2)_{0-100}NR_2R_3$ ,  $-NH(CH_2)_{0-12}CONH(CH_2)_{0-100}NR_2R_3$ , or  $-NHR_2$ , where  $R_2$  and  $R_3$  are independently selected from the group consisting of H, Cl, NO, N-acetyl, benzyl,  $C_{1-100}$  alkyl,  $C_{1-100}$  alkylamine,  $C_{1-100}$  alkyldiamine,  $C_{1-100}$  alkylcarboxylate,  $C_{1-100}$  alkenyl, a  $C_{1-100}$  alkynyl, and  $C_{1-100}$  alkyl-L, where L is selected from the group consisting of arylboronic acids, biotins, polyhistidines comprised from about 2 to 8 amino acids, haptens, solid phase supports, oligodeoxynucleotides, N-ethylnitrosourea, fluorescein, bromoacetamide, iodoacetamide, DL- $\alpha$ -lipoic acid, acridine, captothesin, pyrene, mitomycin, texas red, anthracene, anthrnilic acid, avidin, DAPI, and oligodeoxynucleotide, isosulfan blue, malachite green, psoralen, ethyl red, 4-(psoraen-8-yloxy)-butyrate, tartaric acid, and (+)- $\alpha$ -tocopheral;

each X is independently selected from the group consisting of N, CH, and COH;

each a is an integer from 2 to 5; and

each b is an integer from 3 to 6.